Information

Nonneoplastic Disorders of the Parotid Gland

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A wide variety of conditions may be responsible for enlargement of the parotid salivary gland. When confronted with a patient who has parotid enlargement, the initial step is to decide whether this represents a discrete tumor mass or a diffuse swelling of the gland. If a discrete tumor mass is present, treatment is relatively straightforward and usually involves surgical excision. When a diffuse or bilateral enlargement exists, there are many diagnostic possibilities.

The differential diagnosis of such a disorder requires a systematic evaluation of both the salivary glands and the general medical condition of the patient. The nonneoplastic causes of parotid gland enlargement can be broken down into several major types: infectious, systemic and secondary metabolic causes, drug reactions, local causes and miscellaneous (Table 1). These can be broken down further into those conditions affecting either children or adults.

The various causes of parotid enlargement are herein reviewed, and most of the discussion will concern the diagnosis and treatment of the autoimmune class of diseases. It is this group that generally causes the greatest problems both in diagnosis and treatment.

When a patient with parotid swelling is first seen, the most important factor in narrowing down the diagnostic possibilities is getting a complete history. The duration of symptoms and history of pain, fever, swelling with meals, purulent drainage and associated systemic symptoms are obviously critical factors in deciding what initial tests are indicated. Laboratory and radiologic studies are often helpful and will be discussed under specific disease entities, as will various treatment modalities.

Childhood Disorders of the Parotid

Inflammatory disorders in children are divided into viral and nonviral categories, with mumps being the most common cause of parotid swelling in children.

Mumps is an acute, contagious, generalized viral disease that presents as a painful enlargement of the parotid glands. It is spread by airborne droplets of infected saliva. The incubation period is two to three weeks after exposure and its onset is characterized by pain and swelling of one or both parotid glands, which progresses rapidly in two to three days. Local discomfort is exacerbated by stimulation of the gland. A myxovirus can be identified from a specimen of the saliva as long as six days before and up to nine days after the appearance of swelling.[1-3] Other symptoms include fever, myalgia, malaise and headache, which generally last three to seven days. The parotid is the salivary gland involved in 85 percent of the cases. Diagnosis is usually made from clinical findings but viral cultures and serologic tests can be done. A test for serum antibodies to mumps antigens S and V that results in a titer greater than 1:192 indicates recent infection. Laboratory findings are otherwise nonspecific, except for a mild leukopenia. Most mumps infections occur in children and give a lifelong immunity.

Other viral agents causing parotitis have also been identified and produce a clinical course similar to mumps. Parainfluenza viruses 1 and 3, Coxsackie virus A, echovirus and choriomeningitis virus may all cause a parotitis similar to mumps.[2,3]

Bacterial sialadenitis is relatively rare in children and causes symptoms similar to mumps. It may occur either unilaterally or bilaterally. The only initial clinical features differentiating it from a viral source are the presence of purulent salivary secretions and possibly a leukocytosis. Neonatal suppurative parotitis has been described as a separate clinical entity usually occurring between the ages of 7 and 14 days.[2,4] It is usually preceded by a systemic illness that results in dehydration. In this age group, abscess formation is more prevalent, with 20 percent of reported cases requiring external drainage.[2] Bacteria found in these cases are generally *Staphylococcus aureus* (60 percent), with *Escherichia coli, Pseudomonas, Pneumococcus* and *Streptococcus viridans* also being found. The predilection of the parotid gland for these infections is felt to be due to several factors. The slower flow rate of the parotid with the length of Stensen's duct increases the chance for stasis and ascending infections. Additionally, the composition of parotid saliva (the parotid being entirely a serous gland) is a factor because it lacks the bacteriostatic properties found in the mucus-containing secretions of the submandibular and sublingual glands.[2,5]

Chronic recurrent sialadenitis represents the second most common salivary gland disease of childhood. It can occur throughout childhood but is more common in children less than 10 years of age, with the majority being 5 years old or younger.[5] It occurs in one or both glands equally. It usually presents as an acute swelling of the gland that is painful. Unlike acute suppurative parotitis, there is no surrounding erythema of Stensen's duct and only mild if any systemic signs of infection. Laboratory studies may show a mildly raised leukocyte

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ABBREVIATIONS USED IN TEXT

Ig = immunoglobulin
SS-A = nonorgan specific-specific antibody A
SS-B = nonorgan specific-specific antibody B

count, with an increase in the serum total protein due to a rise in the γ-globulin fraction. The swelling lasts from days to weeks and gradually resolves. The secretions from Stensen's duct are often thick and flocculent. *S viridans* is frequently found in cultures. The diagnosis can be suspected by the characteristic clinical course and confirmed by sialography showing sialectasia.[2,5]

Konno[5] studied 52 cases of recurrent parotitis in children using the findings of sialography, biopsy, antibody titers, measured immunoglobulins and long-term outcomes. He found punctate shadows on sialography films in 45 of 52 cases. When these were classified according to number and size throughout the gland, it was found that those patients in whom extensive changes were noted on sialography had experienced frequent recurrences of the swelling and also were younger at onset of symptoms. In 21 cases of unilateral swelling, bilateral sialography was done. In 22 of 27 Konno found changes in both glands, though they were generally less severe in the side without clinical symptoms. Additionally, sialography was done on 18 siblings in 15 cases of recurrent parotitis. He found mild sialectatic changes in 6 of the 18 but stated that in all of these cases in which siblings were studied severe changes were seen on sialograms.[5] Small parotid biopsy specimens were obtained for study in 13 patients. Histopathologic examination of the specimens showed cystic cavities surrounded by small round cell infiltrates with lymphoid follicle formation. The cystic cavities were felt to be constructed from proliferation of the epithelium of the peripheral portion of the interlobular duct or central portions of the intralobular duct with dilation of its lumen.[5]

Immunologic studies comparing serum immunoglobulin (Ig) A, IgG and IgM in 31 patients and 33 controls showed a statistically significant increase only in the IgM fraction in the 3- to 5-year-old age group, as compared with controls. No other statistically significant differences immunologically were found in the patients studied. Long-term follow-up was done on 35 patients who were observed for between 8 and 11 years. Parotid swelling disappeared completely in 21, with 13 patients showing pronounced improvement. Those who did not have sialographic changes initially did better than those with such changes. Follow-up sialography was done on nine patients who had had sialectasia initially; in two, findings had returned to normal, and in six others pronounced improvement of the ductal pattern was seen. One patient who had not improved clinically also showed worsening of the results of his sialography, with conversion into large cystic cavities.[5]

The cause of this disorder is not known. Possible factors include a mild chronic bacterial parotitis due to *S viridans,* which has been isolated from secretions in several series. A hereditary or allergic predisposition has also been considered.[3,6] The possibility of recurrent viral infections was also investigated by measuring—during the acute and convalescent phases—titers to mumps and nine other viruses. Konno[5] found no consistent relationship of the titers with exacerbations of the disease. Findings on examination of the biopsy specimen and sialography are similar to those in Sjögren's disease and this may represent a manifestation of an autoimmune disorder.

Based on their study and long-term follow-up, Konno felt physiologic immaturity of the immune system might play a role in the cause and recurrent nature of the disease. The disease generally resolves or at least abates with age, but in rare instances may progress into adulthood.[2,5]

Sjögren's disease in children is rare, with 21 cases reported in the literature. Its manifestations are similar to that in adults, which will be discussed later.[7] An unusual cause of recurrent parotitis has been reported

TABLE 1.—*Nonneoplastic Causes of Enlargement of the Salivary Glands**

- Inflammatory
  - Acute (specific)
    - Viral (mumps, Coxsackie virus A, echovirus, and lymphocytic choriomeningitis)
    - Bacterial (staphylococcal, streptococcal, pneumococcal, Gram-negative)
      - Acute suppurative of infancy
      - Postsurgical
      - Terminal debilitation
  - Chronic (specific)
    - Tuberculosis
    - Actinomycosis, and the like
    - ?Sarcoidosis
  - 'Recurrent subacute' and chronic recurrent
    - Self-limited
    - Progressive
    - Lymphoepithelial lesion and Sjögren's syndrome
- Systemic and Secondary Metabolic
  - Obesity, hypertension, diabetes mellitus
  - Malnutrition and associated deficiencies (protein, vitamins)
  - Alcoholism and alcoholic liver disease
- 'Hypersensitivity' and Drug Idiosyncrasy
- Local (Salivary Gland) Disturbances
  - Sialolithiasis
  - Sialoangiectasis
  - Trauma, foreign body, fistula
  - Parotid lymphadenopathy
  - Cysts, mucocele and ranula
  - Local duct obstructions (mucous plugs, congenital)
- Miscellaneous
  - Pneumoparotitis
  - Psychogenic
  - Functional overactivity
  - Idiopathic
  - Irradiation sialadenitis

*Reprinted by permission from Batsakis.[1]

TABLE 2.—*Other Causes of Parotid Enlargement**

Nutritional Factors		*Endocrine Factors*	*Drugs*	*Miscellaneous*
Malnutrition	Beriberi	Diabetes	Iodine	Allergy
Alcoholic cirrhosis	Vitamin A-deficient diet	Pregnancy and lactation	Thiouracil	Obesity
Portal cirrhosis	Celiac disease	Menopausal states	Thiocyanate	Heredity
Kwashiorkor	Bacillary dysentery	Thyroid disease	Isoproterenol	Emphysema
Cardiospasm	Chagas' disease	Stress		Idiopathic
Pellagra	Ancylostomiasis			

*Reprinted by permission from Borsanyi.[10]

in children due to chronic cheek chewing with trauma and subsequent stenosis of Stensen's duct.[8]

Parotid Enlargement in Adults

Acute suppurative parotitis in adults is marked by sudden, painful swelling of one or both glands, with fever and leukocytosis. The affecting organism is usually *S aureus* and occurs postoperatively in about a third of the cases. Predisposing factors include debilitation, dehydration and confinement to bed. This may occur in both glands in about 20 percent of cases. Diagnosis is rarely a problem and treatment consists of administering appropriate antistaphylococcal antibiotics and hydration. If the condition does not improve in 48 to 72 hours, then incision and drainage of the gland is indicated.[1-3]

Chronic suppurative parotitis presents as a recurrent, mildly painful swelling, usually associated with meals. Predisposing factors in this disease are a decreased rate of salivary flow, stasis of secretions and alteration in the character of secretions. The initial event may have been an acute infection, though other causes of decreased salivary flow such as mumps, fluid restriction, secondary cardiac disease or drug reactions have also been implicated. This decreased flow leads to stasis and inspissation of secretions resulting in ascending bacterial infection. This leads to sialectasia and chronic acinar destruction. Treatment should be conservative, with hydration and administration of sialagogues and antibiotics for acute exacerbations. If prolonged conservative measures fail, parotidectomy is the only effective surgical management.[2,3] Tympanic neurectomy has been advocated by some but most reports describe erratic results.[9]

Chronic sialectasia may represent a progressive worsening of chronic suppurative parotitis. This disorder is characterized by diffuse swelling of the parotid, progressing during a period of months to years. The postprandial swelling and pain characteristic of earlier disease may no longer be present. Histologically, this has findings similar to Sjögren's disease.[3]

Sialodochitis fibrinosis typically occurs in dehydrated patients. The history is usually of a relatively painless periodic enlargement of the gland with fluid restriction. It is caused by mucous or fibrinous plugs in the ductal system and expression of these plugs from Stensen's duct is diagnostic. Treatment consists of administering sialagogues and massage to extract the plugs.[3]

Obstruction or stricture of Stensen's duct may also lead to intermittent swelling and parotitis. This can be caused by stones or by local trauma to the duct by dentures. Management consists of ductal probing and dilation.[8]

Mycobacterium tuberculosis and atypical mycobacteria may also cause parotid enlargement either as a diffuse enlargement or a discrete mass. Cat-scratch disease and sarcoidosis are also rare causes of parotid enlargement.[2,3] These are mentioned only for completeness and will not be discussed here.

Parotitis may also occur due to administration of various drugs affecting the gland, either directly or as an idiosyncratic response.[1-3,10,11] Iodine causes a diffuse and tender swelling that may occur two to three days after injection of an iodine compound. Atropine sulfate causes enlargement of the gland by its effect on saliva, making it more viscid. Phenylbutazone produces xerostomia in about 20 percent of patients and may also give rise to a parotitis. The phenothiazine and antidepressant groups of medicines also produce xerostomia and possible parotitis on the basis of their anticholinergic effects. Isoproterenol has also been found to cause parotid enlargement, which is felt to be due to chronic sympathetic stimulation of the gland.[7-10] Different antidepressive agents were found to produce different degrees of xerostomia when tested in healthy volunteers. Salivary flow was measured after giving a single drug dose in a double-blind fashion. Administration of lithium and the monoamine oxidase inhibitors produced little change. Amitriptyline hydrochloride, imipramine hydrochloride and pamoate and nortriptyline hydrochloride caused a severe decrease in salivary flow.[11] The thiouracil class of drugs has also been noted to cause parotid enlargement. In most cases, discontinuing use of the drug will relieve the symptoms.

Metabolic Factors

Chronic asymptomatic enlargement of the parotid gland can be caused by a variety of conditions, as outlined by Borsanyi (Table 2).[10] Vitamin deficiencies are known to cause parotid enlargement, though we have seldom seen them in our patient population. Parotid enlargement is seen in 30 percent to 80 percent of patients who have alcoholic cirrhosis. Histologic features of this disorder are swelling of the acinar cells due to an increase in secretory granules, fatty infiltration and fibrosis. Sialography shows a "winter tree" appearance from displacement of ducts from each other by the fatty infiltrate. The cause of the parotitis is not

TABLE 3.—*Associated Findings in Sjögren's Syndrome*

	Sjögren's Syndrome Percent (N = 22)	*Rheumatoid Arthritis and Sjögren's Percent (N = 21)*
Recurrent parotid swelling	81	14
Lymphadenopathy	50	19
Purpura	45	4
Raynaud's phenomena	31	4
Renal	27	0
Myositis	23	0

known, but may be due to a protein deficiency. This condition is virtually nonexistent in nonalcoholic liver disease.

Diabetes mellitus has also been mentioned in association with parotid enlargement; however, the relationship is not as clear as that with cirrhosis. Obesity may also be associated with parotid enlargement due to increased fatty deposits in the gland. The pathophysiology of the parotid enlargement in these disorders is not known.

Autoimmune Diseases

Many patients will have only parotid enlargement or xerostomia, without any history suggestive of infection or obstruction and with no history of taking drugs known to affect the salivary glands. It is in this group of patients that autoimmune disorders are considered, in the spectrum of diseases that have been variously termed Mikulicz's disease or syndrome, sicca syndrome, Sjögren's syndrome and lymphoepithelial lesion. These disorders all produce the same histopathologic change seen in the salivary gland: a lymphoreticular cell proliferation usually associated with atrophy of the acinar parenchyma.

Batsakis[1] defines the terms as follows: Lymphoepithelial lesion refers to end-stage epithelial alteration showing the characteristic lymphocytic infiltration of the salivary parenchyma. Batsakis uses this term to describe a gland that is totally or nearly replaced by chronic inflammatory infiltrate in which only islands of metaplastic ducts are identified. For less advanced lesions in this spectrum, the terms chronic punctate parotitis or chronic nonspecific sialadenitis are used. These pathologic terms refer to the same lesions described by others as the clinical syndromes of chronic sialectasia or sialodochitis fibrinosis.[1] Mikulicz's syndrome is a term used in the past to describe bilateral enlargement of the lacrimal and salivary glands caused by a variety of disorders. This term is no longer preferred by Batsakis for diagnostic purposes. Sjögren's syndrome is characterized by the triad of xerostomia, keratoconjunctivitis sicca and a connective tissue disease, usually rheumatoid arthritis. It is the second most commonly occurring autoimmune disease after rheumatoid arthritis.[12]

The term sicca syndrome may be applied when xerostomia and keratoconjunctivitis sicca occur in the absence of an associated autoimmune disease. The diagnosis can be made on the basis of two of the three features and is classified as primary Sjögren's syndrome if no systemic disease is present and secondary if a connective tissue disorder is associated. This disease affects primarily women and is usually first noted in middle age. In most patients the disease runs a rather benign course manifested primarily as exocrine gland impairment. The diminution of lacrimal gland secretion leads to destruction of the corneal and conjunctival mucosa, with the findings of punctate corneal abrasions on fluorescein staining. Parotid enlargement is seen in about 80 percent of patients.[12] Xerostomia with diminished taste, mucosal ulceration, difficulty swallowing and increased dental caries are usually the major symptoms in a patient. Exocrine gland involvement of the rest of the upper respiratory tract may lead to chronic dry cough, hoarseness and bronchitis. About a fourth of patients will have extraglandular involvement, with lymphoid infiltration in the reticuloendothelial system, kidneys, muscles and lung.[12] These lymphoid infiltrates may be benign or malignant. In a study from the National Institutes of Health of observed and expected malignancies in patients who have Sjögren's syndrome, it was observed that such patients have a relative risk of lymphoma 43 times that of the normal population.[12] The risk to patients who do or do not have associated rheumatoid arthritis was similar. In patients who have Sjögren's disease with or without parotid swelling, the group with parotid swelling showed an increased risk of 66 times compared with 12 times in those with no parotid swelling. In this same study, three cases of Waldenström's macroglobulinemia developed. As this is a very rare disease, no incidence rates were available in the general population. However, the risk in Sjögren's syndrome was felt to be much greater than in the general population.[12]

The clinical course of patients with Sjögren's syndrome and rheumatoid arthritis is different from those who have primary Sjögren's. Moutsopoulos and coworkers[12] compared the clinical course of 43 patients who had Sjögren's syndrome (21 who had rheumatoid arthritis and 22 who had Sjögren's alone) in which there was a follow-up period of at least five years. Diagnosis of rheumatoid arthritis antedated the diagnosis of Sjögren's syndrome by 2 to 40 years in 16 of the 21 patients. No difference was found in the biopsy results or laboratory studies of these patients; striking differences were found, however, in the clinical manifestations.

A recurrent parotid swelling was found more often in patients with Sjögren's syndrome alone than in those who had Sjögren's and rheumatoid arthritis (Table 3). In addition, lymphadenopathy, purpura, Raynaud's phenomenon, renal involvement and myositis occurred more often in patients who had only Sjögren's than in patients who had rheumatoid arthritis and Sjögren's. There was no difference found in the incidence of pulmonary involvement with lymphoma or Waldenström's macroglobulinemia between the two groups of patients.[12]

Laboratory data on patients with Sjögren's syndrome also show differences depending on the presence or absence of rheumatoid arthritis. Of those with primary Sjögren's syndrome, 80 percent will have an increased sedimentation rate. Anemia and leukopenia occur in less than a third. More than 75 percent of the patients will have a hyperglobulinemia and numerous autoantibodies, such as rheumatoid factor, antisalivary duct antibody, antinuclear antibody and antibodies to extractable nuclear antigen.[12] There are currently four autoantibodies known in Sjögren's syndrome[2,3]: the organ-specific antisalivary duct antibody similar to the antithyroid antibody found in Hashimoto's disease and three nonorgan specific systems. These were discovered in the early 1960s. Antisalivary duct antibody is usually an IgG; its presence is inversely correlated with the degree of lymphoid infiltration, that is, those with more extensive lymphoid infiltration do not have the antibody. It was found in 69 percent of those patients who had rheumatoid arthritis and secondary Sjögren's syndrome, but in only 25 percent of those who had primary Sjögren's or who had rheumatoid arthritis without evidence of Sjögren's syndrome. The three nonorgan specific-specific antibodies are call SS-A, SS-B and rheumatoid arthritis-associated nuclear antigen. The antibodies against these three markers are found in different percentages of patients who have primary Sjögren's, Sjögren's with rheumatoid arthritis and Sjögren's with systemic lupus erythematosus. Patients who have Sjögrens syndrome alone tend to have anti-SS-B and anti-SS-A antibodies but not antisalivary gland antibody or rheumatoid arthritis nuclear antigen. Those who have Sjögren's syndrome and lupus have anti-SS-B. Patients who have Sjögren's and rheumatoid arthritis have antisalivary gland antibody but not the anti-SS-A or anti-SS-B antibodies. Differences in the histocompatibility loci (human leukocyte antigen) have also been examined in patients who have Sjögren's syndrome and those who have Sjögren's and rheumatoid arthritis.[12] Although studies have been done in only a small number of patients, differences between the human leukocyte antigen loci found in the normal population differed from those who have Sjögren's. Again, there were differences between those who have primary Sjögren's and Sjögren's with rheumatoid arthritis. These loci are hypothesized to control the immune response that causes the lymphoid infiltration of the salivary glands.[12]

As can be seen by the overlap of the above tests, these do not yet represent the definitive diagnostic answer to Sjögren's syndrome. What, then, is a reasonable and generally available battery of tests that can be used to evaluate a case involving parotid enlargement and xerostomia? As has already been alluded to, a comprehensive history and physical examination, including drug and nutritional history, are obviously important. Laboratory studies that should be done include a complete blood count, a sedimentation rate, quantitative immunoglobulins, antinuclear antibody, anti-DNA, rheumatoid factor and a chemistry panel. Most patients who have Sjögren's will show a hyperglobulinemia, usually broad-based and primarily IgG. Anti-DNA and antinuclear antibodies have been found in 10 percent of patients. Positive findings are supportive but certainly not diagnostic of Sjögren's syndrome. Of the four specific antibodies previously discussed, the SS-A, SS-B and rheumatoid arthritis nuclear antigen can be identified by sending specimens to the Scripps Reference Laboratory, 505 South Coast Blvd, La Jolla, California. The antisalivary duct antibody test is not yet available.

Ophthalmologic examination should include Schirmer's test (for keratoconjunctivitis sicca) and also fluorescein or rose-bengal staining for corneal abrasions. A Schirmer's test finding of less than 5 mm of tearing in five minutes is considered abnormal.[13,14]

Salivary flow measurements and sialochemical analysis can also be done. Sialochemical analysis will generally show an increase of the sodium and also IgA and IgG concentrations. This test is hindered somewhat by the fact that in one series an adequate specimen of saliva could only be obtained in about 30 percent of patients who had xerostomia.[14]

By far the two most widely used methods of diagnosis of Sjögren's disease are sialography and labial biopsy of the minor salivary glands. Sialography will show varying degrees of sialectasia, which is certainly not unique to Sjögren's but when correlated with the clinical history can strengthen the clinical diagnosis. The labial biopsy of the minor salivary glands still represents the surest diagnostic test for Sjögren's syndrome. The results will be abnormal in about 70 percent of the cases in patients manifesting symptoms of Sjögren's syndrome.[1] The histologic findings are atrophy and loss of acinar tissue with distortion of the lobular architecture. Lymphoid infiltration—sometimes accompanied by germinal center formation—and ductal changes including hyperplasia of the lining cells with the development of myoepithelial islands are seen. As with the disease process itself, the biopsy results show a varying degree of lymphoid change, depending on the disease state. The epimyoepithelial island that is characteristic for the disease is rarely seen on the labial biopsy specimens.[1]

Greenspan[15] attempted to quantitate the biopsy results by grading them according to the amount of lymphocyte invasion. He graded these on the basis of foci of lymphocytic invasion per 4 sq mm, with a focus being defined as 50 or more lymphocytes, histiocytes or plasma cells in one aggregate. He then examined biopsy specimens from 75 patients and additionally 53 postmortem specimens from patients who had not had Sjögren's syndrome. He found a grade 4 on biopsy specimens (more than one focus per 4 sq mm) only in those patients who were felt to have definite Sjögren's syndrome. A variable number of foci were found correlating with the degree of clinical symptoms. On the basis of his findings, Greenspan felt a grade 4 result on the biopsy specimen was diagnostic of Sjögren's syndrome.[15]

Rarely, other disorders may give an identical appearance to Sjögren's and be found only on examination of

a biopsy specimen. Amyloidosis and hemochromatosis have been reported as causes of xerostomia, diagnosed by labial biopsy.[16,17]

Treatment

Treatment of acute suppurative parotitis is straightforward and has already been mentioned. The present treatment of Sjögren's syndrome as it affects the oral cavity is symptomatic. Hormone therapy and administration of vitamins, autonomic drugs and steroids have all been used with little success. Xerostomia has been treated symptomatically by increased fluid intake and promoting salivation by chewing gum or sucking hard candy. Taking sialagogues such as SSKI (saturated solution of potassium iodide) or a solution of citric acid may occasionally be helpful, usually in the milder cases that still respond to stimulation. In these cases, repeated stimulation for one to three months may give long-term relief.[8] An artificial saliva substitute or glycerine-containing mouthwash may also be used. Meticulous dental care is essential to diminish the tendency for dental caries to occur due to xerostomia. Steroids have been used with limited success during the exacerbation of parotid swelling.

Another mode of therapy has been proposed based on the theory that the cause of Sjögren's syndrome is a lack of synthesis of prostaglandin E_1. Horrobin and Campbell[18] base this theory on several factors: prostaglandin E_1 seems to play a role in the regulation of salivary and lacrimal secretions; prostaglandin E_1 is essential for normal function of T-lymphocytes; it is an antiinflammatory agent; vitamin C deficiency inhibits prostaglandin E_1 synthesis, and Sjögren's may occur in pyridoxine deficiency.

The aim of treatment is to raise endogenous prostaglandin E_1 production by administering essential fatty acid prostaglandin E_1 precursors, pyridoxine and vitamin C. A preliminary trial using efamol, an oil high in linoleic acid, vitamin C and pyridoxine, has been undertaken. No controlled studies using this regimen have yet been reported.

Another drug whose use has occasionally been successful is bromhexine.[6,13,19,20] This is a mucolytic agent and is a synthetic derivative of vasicine, an alkaloid from the leaves of *Adhatoda vasica*. This has been tried primarily to increase tear production but has been found in several trials to have a beneficial effect on salivation. One study showed a significant increase in tearing, as measured by Schirmer's test in about 70 percent of patients. Its effect on salivary flow has been studied by using sialochemical analysis before and after treatment. Immunoglobulin and electrolyte measurements were made, as elevated sodium, IgA and IgG levels have been found in Sjögren's syndrome.[14] One study showed a decrease in IgA and sodium values with bromhexine administration but could not find any change in salivary flow.[13,19] Other studies have shown no objective improvement in flow rate, with a subjective improvement no better than in control groups using a placebo.[20] This drug has been reported on in European medical journals but is not yet available in the United States.

To illustrate the difficulties in establishing a definitive diagnosis, two cases are presented.

Reports of Cases

CASE 1. This is a 50-year-old woman who had a three-month history of parotid swelling on both sides, described as minimally tender with initially some increase in tenderness with eating. She said she had no noticeable dryness in her mouth. Her medical history was unremarkable, with no history of significant alcohol intake, diabetes, thyroid problems or arthritis. On physical examination there was bilateral, nontender, diffuse parotid enlargement with clear saliva expressed from both Stensen's ducts. The rest of the physical examination showed no abnormalities and a Schirmer's test was normal. Laboratory studies were remarkable for the findings of a sedimentation rate of 60, a serum total protein level of 8.9 grams per dl (normal 6.0 to 7.8), with an elevated IgG fraction and a positive test for rheumatoid factor. A chest x-ray film was normal. Labial biopsy and sialography were done and the results of both were normal.

CASE 2. The patient is a 69-year-old woman who for nine months had had left facial swelling and dryness in her mouth. This began following a flulike illness. Her major symptom was that of dryness, which made it difficult to eat and had resulted in a diminution of her taste. Her medical history was entirely unremarkable. On physical examination there was thick, stringy mucus expressed from the left Stensen's duct. A Schirmer's test gave abnormal results, showing less than 5 mm of tearing in five minutes. Ophthalmologic examination showed no evidence of corneal ulcerations. Laboratory studies disclosed entirely normal values. A sialogram showed punctate sialectasia of the left parotid gland and a labial biopsy specimen showed lymphocytic infiltration and acinar atrophy.

The history and laboratory findings in case 1 suggested Sjögren's syndrome, except for normal findings on a biopsy and sialogram. The patient does not meet the diagnostic criteria for Sjögren's at present and is currently being observed for any change in her symptoms.

Case 2 was interesting in that the patient dated the onset of her symptoms to a flulike illness. The lack of eye findings or evidence of an autoimmune disorder would place her in the category of chronic sialectasia with a possible viral cause.

Summary

The parotid gland may be affected by a variety of disease processes that all similarly result in enlargement and xerostomia. The limited response of the salivary glands to a multitude of insults makes diagnosis difficult. A review of some of the more common nonneoplastic disorders of the parotid gland has been

presented, along with appropriate diagnostic and treatment modalities.

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